ABSTRACT

Disclosed are methods and compositions for the identification, characterization and inhibition of farnesyl protein transferases, enzymes involved in the farnesylation of various cellular proteins, including cancer related *ras* proteins such as $p21^{ras}$. One farnesyl protein transferase which is disclosed herein exhibits a molecular weight of between about 70,000 and about 100,000 upon gel exclusion chromatography. The enzyme appears to comprise one or two subunits of approximately 50 kDa each. Methods are disclosed for assay and purification of the enzyme, as well as procedures for using the purified enzyme in screening protocols for the identification of possible anticancer agents which inhibit the enzyme and thereby prevent expression of proteins such as $p21^{ras}$. Also disclosed is a families of compounds which act either as false substrates for the enzyme or as pure inhibitors and can therefore be employed for inhibition of the enzyme. The most potent inhibitors are ones in which phenylalanine occurs at the third position of a tetrapeptide whose amino terminus is cysteine.